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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/521,669	11/08/2005	Hesson Chung	HANO-001	9231

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EXAMINER	
PALENIK, JEFFREY T	

ART UNIT	PAPER NUMBER
1615	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/521,669	CHUNG ET AL.	
	Examiner	Art Unit	
	Jeffrey T. Palenik	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 May 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5,6,10-13,16,27-33,37,38,42,43,48-51,54 and 65-74* is/are pending in the application.

4a) Of the above claim(s) *16,28-33,37,38,42,43,48-51,54,65-71 and 74* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5,6,10-13,27,72 and 73* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 January 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8 Nov 2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

RESPONSE TO REMARKS

The Examiner thanks the Applicants for their timely reply filed on 22 May 2008, in the matter of 10/521,669.

Applicants' election **with traverse** of Group I (claims 1, 5, 6, 10-13, 16, 27, 72 and 73) is acknowledged. Applicants' elections of the following species **with traverse** is also acknowledged: insoluble drugs, anti-cancer drugs and paclitaxel derivatives. Applicants request reconsideration of the lack of unity requirement on the grounds that the invention to Gao et al. (USPN 6,531,139) necessitates the use of diglycerides in its formulation whereas the claims to the instant invention do not.

Applicants' request for reconsideration of the lack of unity requirement has been fully considered by the Examiner, but **is not persuasive** because Applicants are arguing limitations which are not in the claims. The Examiner agrees with Applicants on the point that Gao does necessarily teach using diglycerides as part of the practiced formulation. However, the instant claims do not necessarily exclude the use of diglycerides within the composition. The instant claim 1 is directed to a composition ***comprising*** percentages of at least one monoolein, of an oil, and of paclitaxel. The fact that the monoolein component taught by Gao happens to be admixed with diglyceride is irrelevant; a percentage of compositional monoolein is still taught.

Applicants' elections of Group I and the aforementioned species thus stand and are made **FINAL**. The claims of Groups II-VI, as well as claim 16 from Group I, are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to non-elected

inventions, there being no allowable generic or linking claim. Applicants timely traversed the restriction requirement between the compositions and methods.

The remaining claims 1, 5, 6, 10-13, 27, 72 and 73 are presented and represent all claims under consideration.

INFORMATION DISCLOSURE STATEMENT

An Information Disclosure Statement (IDS), filed 8 November 2005, is acknowledged and has been reviewed.

SPECIFICATION

The abstract of the disclosure does not commence on a separate sheet in accordance with 37 CFR 1.52(b)(4). A new abstract of the disclosure is required and must be presented on a separate sheet, apart from any other text.

CLAIM REJECTIONS - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 5, 6, 10-13, 27, 72 and 73 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claims 1, 5, 10 and 73, percentage ranges for each of the components are recited using the symbol "~". Recitation of the ranges using said symbol renders the claims

indefinite because the symbol has a well-known connotative definition of meaning "approximately" or "about". Thus is it is unclear exactly what compositional ranges Applicant is reciting.

The remaining claims are rejected since they depend from rejected claims.

CLAIM REJECTIONS - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the

time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 5, 6, 10-13, 27, 72 and 73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gao et al. (USPN 6,521,139).

The instant claims are directed to a mucoadhesive formulation comprising, by weight, 4-90% of at least one monoolein compound, 0.01-90% of an oil and 0.01-20% of paclitaxel, wherein the ratio of monoolein to oil is greater than 1:1 (claim 1). Claim 73 further limits the composition of claim 1 such that it narrows the percent ranges of each of the claimed components. Additional limitations to the oil component are recited in claims 5 and 6. The composition is recited as further comprising 0.01-5% of an additive such as the elected paclitaxel derivatives, which are insoluble, anticancer drugs (claims 10-13). The administration route limitation in claim 27 is considered by the Examiner to be a recitation of intended use, since said limitation does not serve to further limit the actual composition. Claim 72 recites that the formulation be either liquid or semi-solid.

Gao et al. teach a pharmaceutical composition comprising a pharmaceutically active agent, a glyceride mixture consisting essentially of diglyceride and monoglyceride, one or more pharmaceutically acceptable solvents and one or more pharmaceutically acceptable surfactants (claim 1). The glyceride ratio is further taught in claim 1 as ranging from about 9:1 to about 6:4 by weight. Claims 8 and 10 respectively teach that the monoglyceride is monoolein and that the di-/monoglyceride compound exists in the composition in an amount between about 5% to about 40% by weight. Given that the monoglyceride portion of the glyceride component is taught as ranging from about 10-40% and that the overall glyceride

component ranges compositionally from about 5-40% by weight, it follows that said monoglyceride is taught as being in the composition ranging overall from about 0.5% to about 16% by weight. Triacetin, which is a triglyceride compound whose branches each have 2 carbon atoms, is taught as a surfactant in claim 1. Claim 19 further teaches the surfactant as being present in the composition between about 10-50% by weight. Claims 2 and 5 teach paclitaxel and its derivative, docetaxel, as active agents and that said active is present in the composition between about 5-30% by weight, respectively. The composition is further and preferably taught as taking the form of a liquid for the purposes of preparing soft elastic gelatin capsules for oral administration (col. 9, line 66 to col. 10, line 4).

Gao et al. do not expressly teach: (1) the ratio of monoolein to oil as being greater than 1:1, (2) paclitaxel derivatives as additives or in combination with paclitaxel, (3) the claimed additive percent range, or (4) the narrower claimed compositional percent ranges of claim 73.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a composition comprising at least one monoolein, an oil, paclitaxel, and an additional additive in the form of a paclitaxel derivative, as suggested by Gao, modify the amounts and/or ratios of the ingredients, and produce the instant invention in a liquid format for use in an orally administered form.

One of ordinary skill in the art would have been motivated to do this because Gao expressly teaches a preparing a composition wherein the active agent is paclitaxel or one of its derivatives, such as docetaxel, in addition to the other aforementioned components. Preparation of the composition as a liquid for downstream use in a soft gelatin capsule format

is also preferred. Regarding the additive, though it is not expressly taught that the paclitaxel derivative docetaxel is used in combination with paclitaxel as an "additive", it would have been *prima facie* obvious to combine the two compounds within the same dosage form as both are taught in the art (e.g. claim 2) and as being used for the same purpose. The idea of combining the two compounds flows logically from their having been individually taught by Gao et al. (see MPEP §2144.06). *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980)

Furthermore, while the reference does not expressly teach all of the percent ranges (e.g. claim 10 and 73) or the greater than 1:1 ratio of monoolein to oil, as claimed by Applicants, the values and formats of each parameter with respect to the claimed composition are adjustable. It thus follows that each is a result-effective parameter that a person having ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. In the instant case, it would have been within the purview of the skilled artisan to adjust the amounts of both the monoolein and/or triacetin (oil triglyceride) compounds used in the composition in order to achieve a ratio of the two equating to greater than 1:1 (see MPEP §2144.05(II)(B.)). Similarly, it would have been customary for an artisan of ordinary skill, to further narrow the claimed compositional percentages, in order to achieve the desired formulation for solubilizing paclitaxel. Thus, absent some demonstration of unexpected results from the claimed parameters, optimization of any of these parameters would have been obvious at the time of Applicants' invention.

From the teachings of the reference, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the reference, especially in the absence of evidence to the contrary.

DOUBLE PATENTING

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 5, 6, 10-13, 27, 72 and 73 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4, 6, 16-19, and 38 of copending Application No. 10/521,695 (US Pre-Grant Publication No. 2006/0127420). Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending claims of the '695 application are obvious

variants, if not anticipatory, of the currently presented claims. The subject matter recited by both the instant claims 1 and 73 is combined within and read upon by claims 1-4 of the '695 application. Instant claims 5 and 6 are read on and anticipated by copending claim 6 regarding the specific triglyceride and oil components, specifically the compound triacetin. Instant claims 10-13 are read on and anticipated by copending claims 16-19 regarding the additive limitations. Instant claims 27 and 72 are read on and rendered obvious by copending claim 38, regarding routes of administration and liquid/semi-solid form limitations, respectively, particularly in view of the fact that the composition is claimed as being for treatment of a bladder tumor, which necessitates the subcutaneous injection of a liquid form of the composition to reach said tumor. The key differences in subject matter between the copending claims and the instant claims is that the claims to the '695 application recite further including an emulsifier as part of the composition (claim 1), in addition to the monoolein to oil ratio limitation (instant claim 1) and the narrower range limitations of the instant claim 73. Despite the aforementioned differences, one of ordinary skill in the art would have immediately recognized the obvious overlap in subject matter and would have been motivated with a high expectation of success, to prepare the instantly claimed composition.

Claims 1, 5, 6, 10-13, 27, 72 and 73 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 26, 28-31, 41-44, 46 and 47 of copending Application No. 10/521,989 (US Pre-Grant Publication No. 2006/0134144). Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending claims of the '989 application are obvious

variants, if not anticipatory, of the currently presented claims. The subject matter recited by the instant claims 1, 13 and 73 are read upon by claims 26, 28, 29 and 41 of the '989 application. Instant claims 5 and 6 are read on and anticipated by copending claims 30 and 31 regarding the specific triglyceride and oil component limitations. Instant claims 10-12 are read on and anticipated by copending claims 42-44 regarding the additive limitations. Instant claims 27 and 72 are read on and anticipated by copending claims 46 and 47 , regarding routes of administration and liquid/semi-solid form limitations, respectively. The key difference in subject matter between the copending claims and the instant claims is that the claims to the instant application specifically recite insoluble, anti-cancer drugs such as paclitaxel (claim 1). Additional differences include the ratio limitation between the monoolein and oil components. Despite the aforementioned differences, one of ordinary skill in the art would have immediately recognized the anticipatory and obvious overlap in subject matter and would have been motivated with a high expectation of success, to prepare the instantly claimed composition.

These are provisional obviousness-type double patenting rejections because the claims in each of the conflicting cases have in fact not yet been patented.

All claims have been rejected; no claims are allowed.

CORRESPONDENCE

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey T. Palenik whose telephone number is (571) 270-1966. The examiner can normally be reached on 7:30 am - 5:00 pm; M-F (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jeffrey T. Palenik/
Examiner, Art Unit 1615

/MP WOODWARD/
Supervisory Patent Examiner, Art Unit 1615